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## *Listeria monocytogenes* septic arthritis in a natural joint: report of a case and review

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In non-pregnant human adults, *Listeria monocytogenes* primarily causes meningitis, encephalitis, or septicemia. Focal infections caused by *L. monocytogenes* are rare, and usually result from a primary bacteremic phase.

We report the case of an 89-year-old male with diabetes mellitus and a long-standing history of bilateral knee arthrosis which had been periodically treated using non-steroidal anti-inflammatory agents. The patient was investigated following an increase in pain from the right knee plus epigastric pain. Gastroduodenoscopy showed hemorrhagic fundal gastritis and three duodenal ulcers. A joint aspirate from the right knee revealed a serosanguineous fluid, and intra-articular corticosteroid injection was performed. Over the following 3 days, the pain increased and radiated to the ankle.

The patient was then admitted to Trousseau Hospital, Tours, France, on 24 December 1996. On physical examination, the patient was alert and oriented. His temperature was 38.2 °C, his pulse was 88/min, and his blood pressure was 135/90 mmHg. The right knee was erythematous and warm, and had a marked effusion. Neurologic examination results were normal. Initial laboratory examination revealed hemoglobin 180 g/L, hematocrit 53, white blood cell count $10.7 \times 10^9$/L (86% polymorphonuclear leukocytes), glucose 8.50 mmol/L, and creatinine 75 μmol/L. A second joint aspirate was performed 3 days after the first, and revealed purulent fluid with a leukocyte count of $13.6 \times 10^9$/L (80% polymorphonuclear leukocytes). Gram-staining of the effusion showed Gram-positive rods. Culture of this fluid yielded small β-hemolytic colonies which were identified as *L. monocytogenes*, serotype 4b, lysovar 1317:340. Culture of the original aspirate also subsequently yielded Gram-positive rods. Manual susceptibility testing (Kirby–Bauer disk method) revealed that the bacterium was susceptible to ampicillin, gentamicin, erythromycin, chloramphenicol, tetracycline, trimethoprim–sulfamethoxazole and vancomycin. Blood cultures were performed but remained sterile. No lumbar puncture was performed, because neurologic examination was normal.

The patient was initially treated with intravenous amoxycillin and trimethoprim–sulfamethoxazole for 7 days; after this, the regimen was changed to intravenous amoxycillin alone. Two weeks after beginning antibiotic treatment, the patient had diarrhea, and *Clostridium difficile* with toxin A was found in his feces. Amoxycillin treatment was terminated and trimethoprim–sulfamethoxazole per os was administered (800 mg every 12 h). The patient was also treated with metronidazole for the following 14 days. After 6 weeks of antibiotic treatment, the septic arthritis had favorably resolved. The patient reported regularly consuming cheese prepared from unpasteurized goats' milk prior to onset of infection.

Septic arthritis is a relatively uncommon manifestation of listeriosis. A review of the English language

**Table 1** Summary of epidemiologic, clinical and bacteriologic data of 18 *L. monocytogenes* septic arthritis cases

| Date | Sex/Age | Underlying disease | Immunosuppressive therapy | Prosthetic joint | Temperature (°C) | Joint involved | Gram stain | Serotype | Antibiotic treatment | Duration |
|---|---|---|---|---|---|---|---|---|---|---|
| 1979 [1] | F/64 | Rheumatoid arthritis | Methotrexate | No | 37 | Right knee | N | – | Ampicillin IV<br>Ampicillin + gentamicin IV | 2 days<br>11 days |
| 1980 [2] | M/66 | Diabetes mellitus | No | No | 36.2 | Right ankle | Y | 1a | Cefoxitin IV | – |
| 1984 [3] | M/77 | Rheumatoid arthritis | Yttrium-90 intra-articular | No | 37 | Right knee | Y | – | Ampicillin IV<br>Ampicillin PO | 10 days<br>6 weeks |
| 1987 [4] | F/37 | Renal transplant<br>Chronic hepatitis | Corticosteroid | Bilateral hip replacement | 36.8 | Left hip | N | 4b | Ampicillin IV<br>Amoxycillin PO | 10 days<br>– |
| 1988 [5] | M/66 | No | No | Left hip replacement (degenerative arthritis) | – | Left hip | – | – | Ampicillin + tobramycin IV<br>Ampicillin IV<br>TMP-SMZ PO | 2 weeks<br>7 days<br>3 months |
| 1989 [6] | M/70 | No | No | Right hip replacement (post-traumatic) | – | Right hip | – | – | Ampicillin + tobramycin IV<br>Amoxycillin PO | 2 weeks<br>– |
| 1989 [7] | M/69 | Rheumatoid arthritis<br>Liver cirrhosis | No | Left prosthetic knee | 36.8 | Left knee | N | – | Ampicillin IV<br>Ampicillin PO | 3 weeks<br>– |
| 1989 [8] | F/64 | Rheumatoid arthritis<br>Cryptogenic liver cirrhosis | Azathioprine | Bilateral knee replacement<br>Bilateral hip replacement | – | Right knee | Y | – | Ampicillin IV<br>Ampicillin + gentamicin IV<br>TMP-SMZ PO | 2 weeks<br>6 weeks<br>18 months |
| 1989 [9] | M/71 | Rheumatoid arthritis | No | Bilateral knee replacement | 38.2 | Left knee | N | – | Ampicillin + gentamicin IV<br>TMP-SMZ PO | 2 weeks<br>4 months |
| 1990 [10] | M/66 | Diabetes mellitus | No | Prosthetic hip (post-traumatic) | 38 | Hip | Y | – | Ampicillin + gentamicin<br>TMP-SMZ PO | 6 weeks<br>– |
| 1990 [11] | M/73 | No | No | Right hip replacement | 38 | Right hip | N | 1/2 | Ampicillin IV<br>Ampicillin PO | 7 days<br>2–3 months |
| 1991 [12] | F/59 | Diabetes mellitus<br>Systemic lupus | – | Prosthetic hip | – | Hip | – | 4b | Erythromycin + gentamicin<br>Tetracycline<br>TMP-SMZ PO<br>TMP-SMZ IV | 17 days<br>3 months<br>4 weeks<br>– |
| 1992 [13] | M/70 | Rheumatoid arthritis | No | Bilateral hip replacement | – | Left hip | – | – | Ampicillin IV<br>TMP-SMZ PO | 9 weeks<br>5 weeks |

**Table 1** *continued*

| Date | Sex/Age | Underlying disease | Immunosuppressive therapy | Prosthetic joint | Temperature (°C) | Joint involved | Gram stain | Serotype | Antibiotic treatment | Duration |
|---|---|---|---|---|---|---|---|---|---|---|
| 1992 [14] | F/64 | No | No | Hip replacement | – | Hip | – | – | Ampicillin IV<br>Amoxycillin PO | 10 days<br>4 weeks |
| 1992 [14] | F/80 | Colonic carcinoma<br>Liver metastasis | No | Knee replacement | – | Knee | – | – | Cefamandole + gentamicin | 9 weeks |
| 1994 [15] | M/29 | Renal transplant | Corticosteroid<br>Azathioprine | Bilateral hip replacement | 38.4 | Right hip<br>Left hip | – | – | Ampicillin IV<br>TMP-SMZ PO | 4 weeks<br>10 months |
| 1995 [16] | F/73 | Rheumatoid arthritis | Corticosteroid | Right hip replacement | 37 | Right hip<br>Right shoulder<br>Left shoulder | – | – | Ampicillin + gentamicin IV<br>Ampicillin IV<br>Amoxycillin | 2 weeks<br>2 weeks<br>– |
| 1997 | M/89 | Diabetes mellitus | No | No | 37 | Right knee | Y | 4b | Amoxycillin + TMP-SMZ IV<br>TMP-SMZ PO | 7 days<br>6 weeks |

Y, positive; N, negative; –, not known; M, male; F, female; TMP-SMZ, trimethoprim–sulfamethoxazole.

literature revealed only 17 other cases. The epidemiologic, clinical and bacteriologic data regarding all the reported cases are shown in Table 1 [1–16].

Of the 18 cases studied, 11 are male and 7 female. Their ages range from 29 to 89 years. Excluding two renal transplant recipients aged 29 and 37 years, the ages of the remaining patients range from 59 to 89 years. In contrast to other causes of septic arthritis, *L. monocytogenes* arthritis affects only older patients. No cases were identified in infants.

Of the 18 patients, 14 had underlying disease likely to result in immunodepression: seven patients had rheumatoid arthritis, four had diabetes mellitus, two were renal transplant recipients, and one had a colonic carcinoma with liver metastasis. Immunosuppressive therapy (azathioprine or corticosteroid) was identified in six of the 18 patients. Immunodepression was identified in 78% of the cases, which contrasts with 16% of patients with other causes of septic arthritis. Rheumatoid arthritis was treated with gold, penicillamine, phenylbutazone, azathioprine or corticosteroid. Diabetes mellitus was diagnosed in four patients, one was not treated (present case), two were treated with tolezamide [15] or insulin [10], and the treatment of the remaining one was not known [12].

Most of the patients had one or more prosthetic joints (14 cases), and the prosthetic joint was always the infected joint. In four cases the prosthetic joint required removal. The joints involved were: hip (10 cases), knee (seven cases), ankle (one case) and shoulder (one case). Two reports underlined the possibility of polyarticular infection [15,16].

Patients' clinical histories often illustrate the difficulty of distinguishing between infective arthritis and activation of the underlying rheumatoid arthritis. Temperature never increased above 38.4 °C and was normal in many cases. In reports where data were available, lumbar and blood punctures were rarely performed; in these cases, cerebrospinal fluid culture remained sterile and blood cultures were almost never positive. Data on leukocyte count in synovial fluid was present in only four cases; in the present case, the leukocyte count of the second aspirate was low, due probably to the corticosteroid injection.

Ampicillin (or amoxycillin) was employed in 15 of the cases, together with an aminoglycoside in seven cases. Since this bacterium is sensitive to these antibiotics, this is the recommended treatment regimen, although trimethoprim–sulfamethoxazole may be a good alternative for the penicillin-allergic patient. One patient described had two episodes of listeriosis that represented infection by the same strain; this case of recurrent listeriosis was due to the patient being given inappropriate antibiotic treatment [12]. The

duration of antibiotic treatment was not less than 6 weeks and some patients received antibiotics for more than 6 months, probably because the prothesis was not removed. Where data were presented, outcome appeared to be favorable with appropriate antibiotic treatment, together with prosthetic removal (four cases), revision of arthroplasty or surgical drainage (four cases). A fatal outcome was not recorded in any of the cases.

In the present case, the severe gastroduodenal lesions caused by non-steroidal anti-inflammatory agents may have allowed the passage of the bacteria through the abnormal gastric membranes. The association of gastroduodenal ulcers and listeriosis is unusual and has never been reported in the literature. We suggest that age and diabetes mellitus, in addition to gastroduodenal lesions resulted in an asymptomatic *L. monocytogenes* bacteremia which seeded the arthritic knee joint.

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## *Escherichia coli* producing a cephamycinase (CMY-2) from a patient from the Libyan–Tunisian border region

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Among Enterobacteriaceae, *Escherichia coli* is usually susceptible to a broad variety of antibiotics. However, strains producing extended spectrum β-lactamases (ESBLs) have been increasingly described during the past decade, mainly in North and South America and Europe [1,2]. We recently encountered a multiply-resistant ESBL-producing *E. coli*, with resistance to ceftriaxone as a hallmark, in a patient transferred from Libya (North Africa) to Switzerland. Because little is known about the epidemiology of resistance to β-lactams in this area, we decided to analyze the mechanism in this isolate.

A 57-year-old European male passenger was struck unconscious and severely traumatized (temporal impression fracture, serial rib fractures, pneumo-hemothorax with emphysema) in a car accident near Sobrata, Libya, on 29 November, 1996. He was given emergency care at a local hospital (Sobrata), and after stabilization of his vital signs he was transferred to Djerba, Tunisia. Initial antibacterial medication included ceftriaxone (1 g b.i.d. IV), gentamicin (80 mg/kg t.i.d. IV), and metronidazole (500 mg t.i.d.